

REMARKS

Introductory Comments

Reconsideration of the above-identified application in view of the foregoing arguments is respectfully requested.

Claims 52-61, 69 and 77-81 are pending and under consideration.

Applicants thank the Examiner for withdrawing the rejection of claims 77-78 under 35 U.S.C. § 112, second paragraph.

Rejection of Claims 57-58, 61, 77-79 and 81 Under 35 U.S.C. § 112, First Paragraph

Claims 57-59, 61, 77-79 and 81 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply to the written description requirement, that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner maintains the rejection made in the previous Office Action. Specifically, the Examiner states that the specification and the claims do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the claimed polypeptides. The Examiner further states that it is only required that a BS322 polypeptide contains at least 50% identity to the polypeptide sequences according to SEQ ID NOS: 24-28 and therefore, that Applicants have not provided the complete structure of a BS322 polypeptide.

Additionally, the Examiner states that Applicants' arguments in the previous Response, with respect to the high level of skill in the art, is not persuasive because specific guidance is required instead of general guidance, and that the genus as claimed, is highly variant.

Applicants respectfully traverse the rejection.

The arguments made in the previous Response are incorporated herein. Additionally, Applicants would like to respectfully point the following out to the Examiner. The claims at issue do not recite the "50% identity" language as the Examiner purports. Therefore, the claims are not drawn to a broad genus of polypeptides as the Examiner purports.

Accordingly, Applicants respectfully request withdrawal of the rejection of claims 57-59, 61, 77-79 and 81 under 35 U.S.C. § 112, first paragraph, as failing to comply to the written description requirement, that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

Rejection of 52-61, 69 and 77-81 Under 35 U.S.C. § 101 and § 112, First Paragraph

The Examiner maintains the rejection of claims 52-61, 69 and 77-81 under 35 U.S.C. § 101 and § 112, first paragraph, as applied in the previous Office Action.

The rejection applying 35 U.S.C. § 112, first paragraph, has been addressed above. Applicants' arguments above are incorporated herein.

With respect to the rejection under 35 U.S.C. § 101, the Examiner contends that Applicants' arguments using the Jager *et al.* reference in the previous Response is not persuasive.

The Examiner reiterates part of his arguments made in the previous Office Action, stating that the nucleotide sequence of BS322, as disclosed in the instant application, is 2683 base pairs in length while the nucleotide sequence of NY-BR-1 as disclosed in Jager, is 4463 base pairs in length. It appears that the Examiner concludes that given the large length difference between these two molecules, BS322 is not a variant of NY-BR-1 and therefore cannot have the same utility as NY-BR-1.

Additionally, the Examiner states that Applicants have presented no evidence that SEQ ID NOS: 24-28 are derived from a single polypeptide that has been shown to be linked to breast disease.

Finally, The Examiner states that Applicants have not provided an adequate written description of the epitopes of the invention because there is no disclosure of a structure-function relationship. The Examiner purports that Applicants have only provided a minimal structure, based on the amino acid sequences as claimed, and a minimal function, based on the epitopes. Therefore, the Examiner concludes that Applicants have not satisfied the written description requirement as discussed in MPEP § 2163.

Applicants respectfully traverse the rejection. Applicants' arguments presented in the previous Responses are incorporated herein. While these arguments have been addressed for the most part in Applicants' previous Responses, Applicants respectfully wish to reiterate the important deficiencies of the Examiner's contentions.

First, with respect to the difference in the nucleotide sequence of BS322 and NY-BR-1, the difference was explained in Applicants' Response dated November 6, 2003. Pertinent sections of the Response are reiterated below:

"As submitted by Applicants in their previous responses, the Dirk Jager *et al.* article "Identification of Tissue-specific Putative Transcription Factor..." support Applicants' contention that SEQ ID NOS: 24-28 as claimed are useful as required by 35 U.S.C. § 101 and § 112, first paragraph. The Jager *et al.* article shows that the gene NY-BR-1 is one of the genes responsible for breast cancer. The gene has 37 exons. See the abstract. Applicants have shown in previous responses in Exhibit A, the 100% alignment match and homology between NY-BR-1 and a nucleotide sequence designated BS322 (SEQ ID NO: 9). Nucleotide sequence BS322 or SEQ ID NO: 9 as described in the instant specification, encodes the polypeptide sequences designated SEQ ID NOS: 24-28. These polypeptides are useful in the detection of breast disease which [the] Examiner has refuted.

The Examiner contends in the previous Office Actions that the alignment match between BS322 and NY-BR-1 does not prove that BS322 is the same molecule as NY-BR-1 since 1143 nucleotides are unaccounted for. The Examiner uses this single basis to support her reason why SEQ ID NOS: 24-28 are not useful in the detection of breast disease. Although Applicants appreciate the Examiner's detailed analysis, Applicants respectfully traverse

the rejection and contend this line of reasoning is flawed for the reason set forth below.

Applicants agree with the Examiner's observation that the alignment consensus between BS322 and NY-BR-1 does not prove BS322 is the exact same molecule of NY-BR-1. However, the 100% consensus between these two molecules over one thousand nucleotides indicates that BS322 could be a splice variant of NY-BR-1. Applicants have attached herein a portion of a BLAST result for AF269087 (NY-BR-1) versus the human genome. As the Examiner can see, the junctions of the exons for the gaps match those that are in the BS322 molecule. Specifically, three exons that account for gaps are at the positions of 3013-3200, 3197-4116 and 2796-3014. This information clearly provides evidence that BS322 is a splice variant of NY-BR-1.

As indicated in the Jager *et al.* article, NY-BR-1 comprises 37 exons. Exons, also known as expressed sequences, are defined as a portions of a gene that appear in both the primary and mature mRNA transcripts (Fundamentals of Biochemistry, Voet *et al.*, John Wiley & Sons, Inc., 1999). Thus, one of ordinary skill in the art would recognize that although BS322 is not the exact molecule of NY-BR-1, the fact that there is a 100% consensus homology between the two molecules for over 1000 nucleotides of the exons indicates that one is a splice of another and would have significant commonalities. It is well known in the art that introns may be excluded from splices which maintain the functionality of a gene. An intron, also called an intervening sequence, is defined in the art as a part of a primary transcript, or DNA encoding it, that is removed by splicing during RNA processing and is not included in the mature, functional mRNA, rRNA or tRNA (Fundamentals of Biochemistry, Voet *et al.*, John Wiley & Sons, Inc., 1999). (emphasis added)."

As shown above, the exact difference between BS322 and NY-BR-1 are previously explained. The fact that NY-BR-1 has 37 exons and the introns were removed from NY-BR-1 in order to obtain BS322, are described above. It appears that the Examiner has a difficult time in accepting this difference of over 1,000 nucleotides. However, Applicants would like respectfully point out to the Examiner that it is common to have a very large number of nucleotides in the genetic code that are introns and are not present in the mature sequence. See Fundamentals of Biochemistry, Voet *et al.*, John Wiley & Sons, Inc., 1999).

On page 831, Voet *et al.* state the following:

"The most striking difference between eukaryotic and prokaryotic structural genes is that the coding sequences of most eukaryotic genes are interspersed with unexpressed regions. The primary transcripts, also called

the pre-mRNAs or heterogeneous nuclear RNAs (hnRNAs), are variable in length and are much larger (~2000 to >20,000 nt) than expected from the known sizes of eukaryotic proteins. ... Thus, pre-mRNAs are processed by the excision of non-expressed intervening sequences (introns), following which the flanking expressed sequences (exons) are joined, or spliced, together.

A pre-mRNA typically contains around eight introns whose aggregate length averages 4-10 times that of its exon. (emphasis added)."

Thus, the over 1,000 nucleotide difference between BS322 and NY-BR-1 is well within the 2,000 to 20,000 difference as noted by Voet *et al.* Additionally, this difference is well within the range length comparison as noted by Voet *et al.* (which states that a pre-mRNA typically contains around eight introns whose aggregate length averages 4-10 times that of its exons).

With respect to the Examiner's contention that Applicants have only provided a minimal structure and a minimal function relationship which do not meet the written description requirement, Applicants respectfully request the Examiner to point out what exactly is "minimal" and where in the MPEP it states that the "minimal" structure and function as provided by Applicants do not meet the written description requirement.

All other arguments made by the Examiner are moot in view of the above responses.

Accordingly, Applicants respectfully request withdrawal of the rejection of claims 52-61, 69 and 77-81 under 35 U.S.C. § 101.

CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. Sections 101 and 112. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Should the Examiner have any questions concerning the above, he is respectfully requested to contact the undersigned at the telephone number listed below. If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

If any additional fees are incurred as a result of the filing of this paper, authorization is given to charge deposit account no. 23-0785.

Respectfully submitted,

Billing-Medel, *et al.*

A handwritten signature in black ink, appearing to read 'Lisa V. Mueller', is written over a horizontal line.

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